MICHIGAN ENVIRONMENTAL SCIENCE BOARD

COUNCIL OF GREAT LAKES GOVERNORS SPECIAL FISH ADVISORY PANEL MEETING SUMMARY

APRIL 7, 1995
RADISSON HOTEL & SUITES
CHICAGO, ILLINOIS

PANEL MEMBERS PRESENT
Dr. Lawrence Fischer, Chair
Dr. Michael Bolger
Dr. Gary Carlson
Dr. Joseph Jacobson
Dr. Martha Radike
Dr. Mark Roberts
Dr. Kendall Wallace
Mr. Keith Harrison, MESB Executive Director

PANEL MEMBERS ABSENT
Dr. Barbara Knuth
Dr. Peter Thomas

DMB/EAD SUPPORT STAFF PRESENT
Ms. Patricia Hiner, Secretary

I CALL TO ORDER

Dr. Lawrence Fischer, Chair, called the meeting of the Special Fish Advisory Panel (Panel) to order at 9:30 a.m.

II EXECUTIVE DIRECTOR'S REPORT

Mr. Keith Harrison, MESB Executive Director, distributed a letter from Dr. Henry Anderson, Wisconsin Division of Health, a memorandum provided by Dr. Milton Clark, U.S. Environmental Protection Agency (USEPA) regarding the calculation of consumption weighted mean percent lipid value for fish consumption for humans, and a 1995 paper on the dietary exposure of mink to carp from Saginaw Bay, Michigan.

III PUBLIC COMMENT

Mr. Daniel Thomas, Great Lakes Sport Fishing Council, addressed the Panel. Mr. Thomas had recently attended a meeting called by the Wisconsin Department of Natural Resources to receive public comment from the charter boat industry regarding the September 1993 *Protocol for a Uniform Great Lakes Sports Fish Consumption Advisory* (Protocol). It was reported at the meeting that Wisconsin would soon implement the Protocol, and that Ohio, Indiana, and Minnesota already had. He also reported a comment made that Michigan's recent relaxation of its advisory could not be justified and that it was a political decision based on many factors. According to Mr. Thomas, the charter boat representatives have negative feelings about implementation of the Protocol. They are concerned that it will have a negative economic impact, not only in terms of tourism and fishing, but also on industry location decisions, with the result being people questioning whether water in the Great Lakes is safe for any purpose.

Mr. Thomas stated that the fisheries industry and the fishing community are being held hostage to achieve some questionable agendas, both at the state and federal levels. He also stated that the Protocol is being driven by fear and intimidation. The states fear retribution by the National Wildlife Federation and the USEPA.

Dr. Fischer commented that Mr. Thomas' information regarding current implementation of the Protocol was of interest since the Panel had previously been told by speakers from the Great Lakes Sports Fish Advisory Task Force (Task Force) that the Protocol was a draft document subject to revision and not intended to be implemented yet.

IV PANEL DISCUSSION ON DIRECTIVES

Following a tentative report outline which the Panel had been working with, Dr. Fischer stated that Mr. Harrison would continue to work on the introduction of the report and that Dr. Radike's summary of all the comments provided to the Task Force on the draft Protocol probably would best fit as an appendix to the report.

Scientific Literature Review and Weight of Evidence

Dr. Wallace indicated that it appears that a thorough review of the literature had been conducted by the Task Force. In terms of the appropriateness of the weight of evidence process, he indicated that the method the Task Force said it used would have been appropriate for setting a Health Protection Value (HPV), but the Task Force deviated from that process and actually based the HPV on expert consensus. He concluded that, while not questioning the expertise of the individual members, an expert consensus prohibits anyone not involved in the process from evaluating how the Task Force arrived at the HPV.

Dr. Fischer expressed concern over the definition of weight of evidence. It appeared to him that the Task Force meant some sort of consensus building process which simply added up all the information regarding harmful effects. Dr. Carlson said that another

term sometimes used is "strength of evidence," and that is how he would classify the Task Force's method. There were differences of opinion among the Panel about whether the Task Force methodology could be classified as risk assessment or risk management.

Dr. Fischer asked Dr. Jacobson whether negative studies or studies showing no toxic effects were given sufficient weight by the Task Force. Dr. Jacobson said that more methodological rigor is required in negative studies. Negatives can be proven, but it is harder. Dr. Jacobson continued by stating that two key aspects to a qualitative weight-of-evidence approach should be soundness of design and clinical significance. According to him, the Task Force weight-of-evidence process did not establish linkage between the HPV and any clinical significance.

Selection of HPV

Dr. Carlson discussed the selection of the HPV. He noted that the term was chosen by the Task Force so it would not be confused with a regulatory term. He concluded that the Task Force did a risk assessment. In his writing, he also discussed the cursory attention paid to the positive benefits of fish consumption. He discussed the weight of evidence approach, agreeing with what had been said earlier by Dr. Wallace, and the difficulty the Task Force had in understanding the concept of "lowest exposure group." A key point according to Dr. Carlson was that the basis for development of the HPV appeared to shift from what the Task Force originally indicated that it was based on, to the rhesus monkey studies and the RfD for 1254, which made it difficult to assess.

Dr. Carlson discussed briefly the Protocol's apparent inability to rapidly modify fish classifications as data change and analytical measurement improves. According to him, because the Protocol proposes using a 3-year average, it would take years to change a classification. Also, creating a standard advisory for the entire Great Lakes region presents the additional problem of not being able to take into account unusual local conditions.

Dr. Fischer directed the discussion back to whether the Protocol was risk assessment or risk management. He questioned whether the HPV was really a health value. The Task Force seems to have lined up a number of regulatory RfDs and selected a value. A RfD is not necessarily a risk value or solely a health-based number. A No-Observed-Adverse-Effect-Level (NOAEL) is derived from hard data, but when a safety factor is added, the process becomes risk management. His objection is that safety factors are applied, but not rigorously defended. Dr. Bolger pointed out that the less that is known about a compound, the more uncertainty and the larger the safety factor. This may be a policy or social value judgement, and so it is actually risk management, although many say it is still scientific. Dr. Jacobson indicated that the use of larger safety factors when less is known is scientifically defensible, using the analog of statistics, where, when a smaller sample size is used there will be a larger margin of error.

Dr. Bolger commented that the USEPA, for instance, has a standard process of defining an RfD and applying uncertainty safety factors, but that such a process is not evident in the Protocol. Dr. Carlson said that the level of the safety factor depends on what information is unknown. A factor of 10 was used commonly in the past, but now it is 3 for Aroclor 1254. The factor of 3 was introduced by Mike Dourson and the Cincinnati USEPA, and is supported by literature articulating its use.

Dr. Bolger indicated that deciding how much protection to provide the public is a policy decision, not a scientific decision. Scientists can estimate the level of protection at various exposure values, but policy makers must decide what level of protection should be afforded. There are several processes that can be used in determining a HPV. The Task Force has used an expert consensus approach. The RfD is another approach. A third approach, and one that has not been used, is to use the dose response and describe the level of risk at each level of exposure. He suggested that the Panel may want to urge the Task Force to derive the HPV using a structured quantitative method, such as the Sielken method.

Dr. Fischer asked Dr. Carlson if he thought it was possible to derive a value for a human NOAEL based on current literature. Dr. Carlson answered that it depended on what was used as an end point. For some end points, data exist; for others, like behavioral effects, data do not. The targets - cancer, reproductive effects, behavioral changes - also need to be identified.

A brief discussion ensued about the reproductive effects of PCBs on mink Dr. Fischer tried to build a Lowest-Observed-Adverse-Effect-Level (LOAEL), assuming that the mink is the species most sensitive to PCBs and that humans are no more sensitive. He argued that what is really needed are data on the threshold effect in a very sensitive species. That would provide a science-based answer, and would avoid the need for unjustified safety factors.

Dr. Jacobson stated that he thought the HPV was defensible for reproductive risk. He considers the weakness of the Protocol is the absence of a scientific basis of extrapolating it to other groups and other risks. Dr. Fischer stated that the reproductive risk factor may be above 0.05.

Dr. Bolger contended that even though there is an apparent risk associated with PCB exposure, what that risk is and what the level of that risk is was not communicated in the Protocol. There is also the issue of the relative importance of this risk as compared to the risks associated with other social practices, for instance, inadequate diets, lead exposure, etc.
Dr. Jacobson stated that there is a sound scientific case concerning the risk of damage to the fetus. Dr. Radike, suggested that an HPV value be set for women of child-bearing age, and another set for adults, children, etc. Dr. Jacobson supported the concept for women of child-bearing age and stated that the North Carolina study showed unequivocally the risk to the fetus. Dr. Fischer indicated that although the relationship found in the North Carolina study between low prenatal dose and fetal

impact can be shown in animal studies, the fact that the North Carolina study never has been reproduced in other human studies casts some doubt. Additionally, the epidemiology and Rogan and Jacobson studies are not consistent in terms of the outcomes. Dr. Jacobson indicated that the data are suggestive enough and internally consistent enough to warrant concern.

Based on its discussion, the Panel concluded that the HPV was not unreasonable for women of child-bearing age in order to ensure the protection of the fetus, but was not scientifically defensible and should not be extrapolated to other segments of the population.

Dr. Jacobson suggested that a recommendation be made by the Panel to apply the margin of safety adjustment at the end of the analysis, rather than continually through the process.

Process Used to Select Chemical Contaminant of Greatest Concern

Dr. Fischer indicated that the Panel had previously agreed that the Protocol's procedure for selection of the chemical contaminant (in this case PCBs) to drive the advisory was not clearly spelled out in the document and therefore not readily reproducible. As a consequence, the usefulness of the Protocol as a tool to develop advisories could become compromised if, in the future, a need arises to change the target chemical contaminant from PCBs, the current chemical of concern.

Uniformity of Monitoring Data

Dr. Fischer indicated that a series of questions were asked of Michigan Department of Natural Resources (MDNR) regarding how it and other Great Lake states sampled fish for health advisories. Based on the response received, Dr. Fischer expressed concern about the lack of uniformity in monitoring data in each state. Sites appear to be chosen with no guidelines, often resulting from public requests. The science of monitoring and selecting samples has not been applied.

Peter Redman (USEPA) explained that in 1984 the Great Lakes states agreed to characterize their fish tissue data by size. Although many different sizes and species of fish were taken in the samples, tissue samples were only compared with like fish (those of equal size). The variations in the samples will not vary significantly.

Dr. Wallace stated that there needs to be a formal cooperative effort among the states to develop a statistically acceptable monitoring and sampling program. The resulting data should be shared between the states and with the Task Force in order that it can review the new data, monitor the three year average and make the assignments of fish among categories. A Protocol could employ valid toxicology information but if PCB exposure to humans derived from inadequate monitoring data are used, the value of the advisory is diminished.

Mr. Harrison indicated that one of the questions asked of the MDNR was whether a formal or informal collaboration existed between it and other states on sampling and monitoring. It was indicated by MDNR that an informal collaboration had been established. Also, the USEPA is currently developing a guidance document for fish sampling and contamination analysis. Both Drs. Wallace and Carlson indicated that the Panel should encourage the formalization of the program in its report.

Assumptions Used to Assign Fish to Consumption Categories

Dr. Wallace discussed the dose reduction factor resulting from the Protocol's advised handling and preparation of fish. According to Dr. Wallace, the reduction value used in the Protocol is 50%, but should probably be 75% based on the supporting data presented in the Protocol. Fifty percent is probably a conservative estimate. Dr. Fischer did not agree and felt comfortable with the 50% value.

The proposed meal size in the Protocol is set at 227 grams of fish for a body weight of 155 pounds. Dr. Wallace questioned whether the aim was the best average/most typical meal or most protective value. According to Dr. Wallace, it appears that when faced with a range, the most conservative number was always chosen by the Task Force, rather than the most representative one. Perhaps meal size should be expressed on a per kilogram body weight basis. Either way, the value should be based on average meal size.

Dr. Wallace questioned the statistical method used in the Protocol in establishing fish size and assigning species. First, there is no explanation as to what "an acceptable level of significance" is, and why 0.6 is chosen as a significant R^2 value. He indicated that a more statistically rigorous and objective method of analysis should be used. Second, Dr. Wallace raised concern with the processes proposed in the Protocol for analyzing and evaluating the sampling data (e.g., potential differences between laboratories in terms of analytical detection level used, and using fish for samples whose sizes are not representative or covered by the advisory). The Panel concurred with Dr. Wallace's analysis.

A brief discussion took place regarding how the Protocol would handle "hot spots", areas where fish contamination was unusually high, and also if the fish monitoring results would be presented on a lake by lake basis or combined for all lakes. The Panel agreed that additional clarification is needed in the Protocol regarding both of these topics.

Sensitivity Analysis

Dr. Bolger stated that his idea of a sensitivity analysis is one that is based on quantitative data. As discussed earlier, the method used in the Protocol to set the HPV value was more of a qualitative analysis. When looking at how the HPV value compares to estimates of exposure, it is important to remember that the estimates of exposure are inherently conservative, especially for the upper percentiles. The

consideration of residual risk has the same problem. The Task Force identified a total diet study that is not based on a statistically-derived exposure estimate (e.g., average) and did not use the most recent data available at the time the Protocol was written. These estimates of exposure are more qualitative in nature and useful for analysis of exposure trends, and should not be compared to other quantitatively based risk figures.

Dr. Bolger also briefly discussed the Protocol's comparison of the HPV estimates of PCB serum levels to reported levels in humans which he indicated was adequately addressed. The Protocol's statement that the cancer risk estimates may over- or under-estimate risks, should be changed to state that it is more likely to be an over-estimation. He recommended the latter because PCB mixtures which more closely resemble the profile found in fish have been shown to be less potent than the 1260 mixture used as the basis for the cancer risk estimate. The cancer potential is more strongly correlated with the more potent PCB mixtures.

Dr. Fischer commented that if an actual sensitivity analysis had been performed in the Protocol, it would be possible to test how each variable in the calculation of the HPV affects the assignment of fish to a given category; determining which variable is most important.

Drs. Fischer and Bolger questioned the Protocol's use of the 1×10^{-4}, as a normally acceptable cancer risk range. Dr. Clark (USEPA) responded that the USEPA recognizes 1×10^{-4} as a standard, but usually prefers 10^{-5} or 10^{-6} for decision making.

Epidemiology Studies and Human Exposure PCB NOAELS and LOAELS

Dr. Roberts commented on whether NOAELs and LOAELs for human exposure to PCB can be derived from occupational and environmental human epidemiology studies. A problem arises with the subset of population that has been traditionally exposed to PCB through occupational exposure. This subset tends to be male dominated, with primarily dermal exposure. Another group of studies, catastrophic exposures such as the episodes in Japan in 1968 and Taiwan in 1979, can also be looked at. These studies involve a more diverse subset of the population than the occupational studies but are often of higher intensity and of shorter duration. These two types of exposures provide some experience to go on, but to use them directly would not be advised since neither is reflective of what is seen in environmental exposure. Furthermore, the Japanese and Taiwanese episodes were dominated by polychlorinated furans and not by PCBs. Finally, the fact that there are gaps in the data should be conveyed in the Panel's report so these areas can be filled and refined.

Dr. Fischer addressed the subject of the heavy loading of PCB's to infants via breast feeding. The loading of PCB's from Great Lakes fish to the adult is small as compared to the loading that occurs to children during their breast feeding years. In addition, and similar to mercury investigations, individuals may have high contaminant levels which cannot be ascribed to fish consumption. Both these examples bring into question fish consumption as the dominant source of exposure.

Dr. Jacobson commented that some of the breast-fed babies had very high blood serum PCB's yet their mothers consumed no Lake Michigan fish. This may suggest that utilization of the mothers body fat in making milk could liberate PCB's which were stored in that fat at a much earlier date. Data on the amount of PCB body fat burden within the general population would be helpful.

Dr. Bolger added that in the 1970's considerable PCB exposure came via poultry and eggs in the 1970's and, in general, the levels have declined considerably from all sources since that time. Diet appears to be the only consistent and recognized source of PCB exposure. This means that the diet of the women studies in the 1970's (Lake Michigan fish eaters), is very different compared to the diet of a similar population today.

Dr. Jacobson indicated that the levels of PCB's in other fats have come down more than they have in fish, but the levels in Great Lakes fish eaters can be expected to be higher than those in the "normal" background public. Babies that are taken off high level breast milk at 1 1/2 years, have blood PCB level back to background levels near the age of 10 1/2. The generation pass-on of PCB's appears not to be a problem after the reduction of exposure.

Immunologic Issues Concerned with Exposure to PCBs

Dr. Carlson commented that USEPA associated Great Lakes fish eating with an experimentally prepared diet containing PCB's, not a diet prepared with Great Lakes fish or fish fat, in order to provide the PCB dosage.

Drs. Jacobson and Carlson questioned the last sentence of Dr. Thomas' draft paper on the immune change imparted by PCB's; it appeared to conflict with the rest of the text. Dr. Bolger indicated that he did not think the conclusion was necessarily inconsistent since all Dr. Thomas was indicating was that the 5 _g/kg was reasonable for the immunotoxin input and not that it was representative of a significant risk.
Dr. Bolger questioned whether the Panel was distinguishing between physiologic response and a toxicological response. According to him, if the response is a toxicologic response, homeostatic capability would be exceeded. While there is evidence to suggest that compensatory effects have occurred, there is no evidence that homeostasis capability was exceeded.

Dr. Fischer questioned the normal variation within the immune system. For instance, are changes that may be seen in the immune system from PCBs and like agents outside of the normal range which would be expected throughout the course of life. According to him, immune response is normally increasing and decreasing based on stress and other factors and he was uncertain if the effects seen in monkeys exposed to PCBs were just a small part of the normal variation or outside of what would normally occur.

Need for Dual Advisory

Dr. Fischer raised the issue of a dual advisory, one for women of child-bearing age and another for the rest of the population. He indicated that Dr. Henry Anderson had stated that a dual advisory would be confusing. Mr. Harrison recalled that Dr. Knuth had stated that she did not believe a dual advisory would be confusing. The Panel concurred that a dual advisory was reasonable.

Dr. Fischer suggested, on the basis of PCBs only, that maybe only one advisory for women of child-bearing age would be appropriate. He went on to express his scientific reservation in accepting a cancer risk assessment for PCBs generated using the USEPA default procedure. Dr. Carlson added that contaminants other than PCB's present in Great Lakes fish should be considered in whether or not to adopt a single advisory for women of child-bearing age. The immune response phenomena has yielded some select responses which altered the immune system makeup, but whether this altering affects the resistance to disease is unknown.

Drs. Fischer and Jacobson expressed their concern with the monkey studies and expressed a need for some other means to determine a more reasonable number. Dr. Fischer went on to indicate that a different cancer risk assessment process, resulting in a different number, could be employed using the average estimated extrapolation line rather than the 5% top of confidence level; however, it was doubtful that the USEPA would accept it.

Dr. Wallace suggested that more weight might be put on the available negative data such as the evidence that heavily PCB-exposed nursing babies showed no ill effects from their mothers' milk then or in later years.

Dr. Fischer stated that to the best of his knowledge and for sure up to two years ago no cancer cases could be directly tied to PCBs, this includes the Yucheng and Yusho exposures. There are no known human data for effect and there may not be a acceptable way to develop a new HPV value. Dr. Roberts concurred stating that PCBs were classified as 2B, potential carcinogens, because of animal studies, but there is no human evidence of carcinogenicity from PCB exposure alone.

Dr. Carlson observed the different end points and dosages used in different studies, notably the relatively high dosages in comparison to normal human food consumption intake. He went on to say that any attempt to come up with a different number than USEPA's 0.05 mg using the same data USEPA used could be futile.

Dr. Jacobson indicated that the Panel is in need of two numbers, one for women of child-bearing age and maybe another for others. The 0.05 mg/kg/day would be fine for women of child-bearing age but the other number for the rest of the population is a problem. He suggested that a reasonable HPV number could be derived from using an RfD approach for cancer given that PCBs are not genotoxic or extrapolating from the exposures that the breast-fed children got in Michigan and North Carolina. In the Michigan study, all of the fetuses exposed to a high dosage displayed some deficiencies at birth, but those same babies displayed no additional degeneration of their fetal deficiencies and no new deficiencies appeared even when they were being given triple

their fetal dose via their mothers milk. In Germany, a cross-fostering rat study was conducted which showed the same pattern; prenatally exposed pups showed deficits on several neurobehavioral outcomes while the post-natally exposed rats did not. As a consequence, there is a corroboration of the results between a human and an experimental manipulation animal study.

It was decided that Dr. Fischer would consult with selected Panel members to see how feasible it would be for the Panel to develop a second HPV. A second alternative might be to inform the Task Force through the report of the rationale for having two HPVs, provide them some guidance on their development and then suggest that they develop them.

Health Benefits

Dr. Fischer brought up the subject of the health benefits of eating fish, namely the omega three fatty acids. He stated there was evidence that ingestion of these fatty acids is antiarthrogenic, reduces serum triglycerides, assists antihypertension drugs and may reduce blood cholesterol. There is evidence that fish consumption enhances visual and neuro development in babies. Based on the literature, the uncertainty level is much less for the benefits of eating fish than it is for estimates of the risk from consumption of fish. He indicated that he would continue to collect data on this topic.

Drs. Fischer and Jacobson expressed their need to have Dr. Barbara Knuth's views on how best to approach the presentation of an advisory which addresses both risks and benefits of eating fish.

Mr. Redman (USEPA) stated that of all the state fish advisories issued in the past, the public dislikes the Michigan advisory the most and favors the advisories issued by Minnesota and Ontario (USEPA protocol). The latter advisories allow the anglers to make a judgement on the fish they just caught.

Dr. Fischer stated that the objective should be to provide the public with accurate information, not easy numbers that have no justification. Dr. Jacobson added that there are two issues, one the ability to communicate uncertainty (in the text) and secondly, to communicate that uncertainly to the greatest public.

Mr. Harrison requested that all the Panel members send copies of the references cited in their papers to him to complete the files and to allow him to make them available to the rest of the Panel.

V ADJOURNMENT

The meeting was adjourned at 4:00 p.m.

Keith G. Harrison, M.A., R.S., Cert. Ecol.
Executive Director
Michigan Environmental Science Board